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Registration Decision RD2012-34

Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites

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Registration Decision for Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is granting full registration for the sale and use of Phostrol 53.6% Fungicide and Phostrol Fungicide, containing the technical grade active ingredient mono- and dibasic sodium, potassium and ammonium phosphites, to suppress or control several fungal diseases on a variety of vegetable and berry crops, as well as outdoor and indoor ornamentals and turf.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

These products were first proposed for registration in the consultation document[1] Proposed Registration Decision PRD2012-11, *Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites*. This Registration Decision[2] describes this stage of the PMRA's regulatory process for mono- and dibasic sodium, potassium and ammonium phosphites and summarizes the Agency's decision, the reasons for it and provides, in Appendix I, a summary of comments received during the consultation process as well as the PMRA's response to these comments. This decision is consistent with the proposed registration decision stated in PRD2012-11.

For more details on the information presented in this Registration Decision, please refer to the Proposed Registration Decision PRD2012-11, *Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites* that contains a detailed evaluation of the information submitted in support of this registration.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[3] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions of registration. The Act also requires that products have value[4] when used according to label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

3 "Acceptable risks" as defined by subsection 2(2) of *Pest Control Products Act*.

4 "Value" as defined by subsection 2(1) of *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

What Are Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites?

Mono- and dibasic sodium, potassium and ammonium phosphites are salts of phosphorous acid. These fungicide active ingredients belong to the Group 33 of the Fungicide Resistance Action Committee and are classified as phosphonates. The mode of action of mono- and di-basic sodium, potassium and ammonium phosphites is both indirect and direct, and involves the induction of host plant resistance and the inhibition of oxidative phosphorylation.

Health Considerations

Can Approved Uses of Mono- and Dibasic Sodium, Potassium, and Ammonium Phosphites Affect Human Health?

Mono- and Dibasic Sodium, Potassium, and Ammonium Phosphites are unlikely to affect human health when used according to label instructions.

Exposure to mono- and dibasic sodium, potassium, and ammonium phosphites may occur when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Mono- and dibasic sodium, potassium, and ammonium phosphites are of low toxicity by the oral, dermal and inhalation routes, minimally irritating to the eyes, and mildly irritating to the skin. The available information suggests that it is unlikely to have any short-term or prenatal developmental effects, as well as any significant genotoxic effects. The precautionary label statement indicating that contact with skin, eyes, and clothing must be avoided, and the personal protective equipment statement that applicators and other handlers must wear a long-sleeved shirt, long pants, gloves, shoes plus socks, and protective eyewear are effective mitigative measures to reduce the risk associated with the use of mono- and dibasic sodium, potassium, and ammonium phosphites.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Dietary risk to humans is considered negligible based on the intended use, long history of use, and low toxicity of the end-use product. The available literature suggests that there is no toxicological concern from ingestion of the end-use product residues.

It is anticipated that the use of mono- and dibasic sodium, potassium, and ammonium phosphites in Canada on food crops will not pose a risk to any segment of the population, including infants, children, adults and seniors, when the foods are subjected to the normal process of washing, peeling and cooking for human consumption. In the United States, phosphorous acid has been designated Generally Regarded as Safe (GRAS) and the potassium salts of phosphorous acid have been exempted from the requirement of tolerance in and on all food commodities when used as an agricultural fungicide on food crops. The United States Environmental Protection Agency (USEPA) introduced an initiative whereby an exemption from the requirement of tolerance was established for ammonium, sodium, and potassium salts of phosphorous acid on all food commodities to permit post-harvest application to stored potatoes at 35 600 ppm or less of phosphorous acid.

Although this end-use product will be used for agricultural crops outdoors, as well as in contained treatment areas, it is not to be applied near or directly to water. No risk due to exposure from drinking water is anticipated.

Risks in Residential and Other Non-Occupational Environments

Bystander exposure is possible from spray drift, but exposure is expected to be negligible if the precautionary label statements are observed.

Precautionary statements (for example, ensuring that the potential for spray drift to areas of human habitation is minimal) on the label of Phostrol Fungicide are considered adequate to protect individuals, children and pets from exposure due to incidental contact with this product.

Occupational Risks From Handling Phostrol Fungicide

Occupational exposure to individuals mixing, loading, or applying Phostrol Fungicide is not expected to result in unacceptable risk when the product is used according to label directions.

Precautionary (for example, wearing of personal protective equipment) and hygiene statements on the label are considered adequate to protect individuals from occupational exposure.

Environmental Considerations

What happens when mono- and dibasic sodium, potassium and ammonium phosphites are introduced into the environment?

The end-use product Phostrol Fungicide, containing mono- and dibasic sodium, potassium and ammonium phosphites, enters the environment when it is sprayed on various crops by in-furrow treatment, ground or aerial applications. It is not expected that mono- and dibasic sodium, potassium and ammonium phosphites will pose a risk to non-target terrestrial and aquatic species given its low toxicity to these organisms.

Value Considerations

What Is the Value of Phostrol Fungicide?

Phostrol Fungicide is a non-conventional alternative fungicide with systemic properties that may be integrated in a spray program for suppression or control of several diseases on a wide range of crops.

Major diseases suppressed or controlled by Phostrol Fungicide include phytophthora root rot on raspberries, late blight and pink rot on potatoes as well as downy mildew on grapes. Phostrol Fungicide also has a low risk of resistance development, which makes it a viable option for the management of certain high-risk pathogens.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Phostrol Fungicide to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because mono- and dibasic sodium, potassium, and ammonium phosphites are used for formulating a commercial product, the statement in the precaution section on the Phostrol 53.6% Fungicide label, "prevent access by unauthorized personnel", will help mitigate the inappropriate use of the product, and help avoid exposure. Other precautionary statements on the technical and end-use product labels, such as: "avoid breathing vapors or spray mist, avoid contact with eyes; remove contaminated clothing and wash clothing before use; applicators and other handlers must wear protective eyewear, long pants and long sleeved shirt, waterproof gloves, and shoes plus socks," should be effective in minimizing the potential for exposure.

Other Information

The relevant test data on which the decision is based (as referenced in PRD2012-11, *Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites)* are available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa). For more information, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra.infoserv@hc-sc.gc.ca).

Any person may file a notice of objection[5] regarding this registration decision within 60 days from the date of publication of this Registration Decision. For more information regarding the basis for objecting (which must be based on scientific grounds), please refer to the Pesticides and Pest Management portion of the Health Canada's website (Request a Reconsideration of Decision, http://www.hc-sc.gc.ca/cps-spc/pest/part/protect-proteger/publi-regist/index-eng.php#rrd) or contact the PMRA's Pest Management Information Service.

[5] As per subsection 35(1) of the *Pest Control Products Act.*

Appendix I Comments and Responses

Comment # 1: The commenter requested the source of information from which the mode of action of Phostrol Fungicide was described by the registrant, as they believed the source of this information was from a proprietary study. In addition they requested that if the mechanism of the mode of action cannot be substantiated, then all references to the mode of action should be disallowed.

PMRA Response: The publically-available references below substantiate the registrant's claim that the mode of action is generally considered to be unknown but that it includes the induction of plant host resistance, and inhibition of oxidative phosphorylation.

Fungicide Resistance Action Committee. FRAC Code List: Fungicides sorted by mode of action (including FRAC Code numbering). (2009). pp 10. PMRA # 1875162.

Smille, R. B.R. Grant and D. Guest. 1989. The mode of action of phosphite: Evidence for both direct and indirect modes of action on three *Phytophthora* spp. in plants. Phytopathology 79: 921-926. PMRA # 1875162.

Comment # 2: The commenter expressed concern that the Phostrol Fungicide claim of control of pink rot (*Phytophthora erythroseptica*) on post-harvested potatoes was supported based on unacceptably minimal evidence (four efficacy trials, with assessments made after 21-30 days in storage). A comparison was made to a similar phosphorus acid-based product with a similar potato post-harvest claim, where the PMRA requested more extensive data requirements than for Phostrol Fungicide. In addition, the commenter questioned why the level of disease management was supported at "control" level for Phostrol Fungicide, while only at "suppression" for the other phosphorus acid-based product.

PMRA Response: The PMRA assesses value evidence for each product individually, reviewing the information that was submitted at the time of the review, and does not refer to data from previous applications for comparison purposes. While phytotoxicity on a crop or commodity may have been a concern for a previously-reviewed phosphorus acid-based product, no adverse effects were noted during the value review for Phostrol Fungicide. The quality (not just quantity) of efficacy trials, the disease pressures present during the trials, plus additional supporting evidence (scientific rationales, use history from the product used elsewhere in the world) all factor into a decision to support a claim or not, or to ask for additional use information on a claim. In addition, as of November 17, 2010, the PMRA is implementing a more flexible approach to assessing product claims as a result of Regulatory Proposal PRO2010-07, *Value Guidance – Benefit Information and Use History*. Therefore, each crop and disease claim is assessed based on efficacy data, supplementary evidence, scientific rationales, use history and benefits information submitted and available for review at that time, with emphasis on the value of each proposed claim for growers. It is the PMRA's opinion that sufficient evidence was submitted to address the value concerns for this crop and disease claim for Phostrol Fungicide.

With respect to supporting a claim of suppression or control of a particular disease, in general, the value evidence must support product efficacy at a level of between 80-100% for the claim of pest control. Based on the value evidence reviewed, the Phostrol Fungicide claim for control of pink rot (*Phytophthora erythroseptica*) on post-harvested potatoes will remain supported at the level of control.

Comment # 3: The commenter expressed concern that the PMRA-approved claim for suppression of pink rot (*Phytophthora erythroseptica*) on potatoes when Phostrol Fungicide is applied once as an in-furrow application was supported based on unacceptably minimal evidence. The commenter indicated that it is their belief that it should be total application load of phosphite that should be considered, and one application is not sufficient to control the disease. They submitted efficacy trials based on a similar phosphorus acid-based product with a similar potato post-harvest claim. The commenter requested that this claim not be supported for Phostrol Fungicide, and additional value information should be provided before this claim can be supported.

PMRA Response: The PMRA assessed the Phostrol Fungicide value evidence submitted for this claim, and partially agree with the position of the commenter. Only one trial was submitted using this application method, and the disease pressures in the study were considered low. However, the registrant of Phostrol Fungicide requested the claim of 'suppression' and not 'control' (which would require demonstrating a higher level of disease management), and the study results indicated that there was value to making a single application in-furrow, with sufficient disease management to be considered 'suppression' under low disease pressures. In addition, since only one study was submitted and consistency in product performance should be demonstrated, additional confirmatory value evidence was requested as a condition of product registration (as indicated in PRD2012-11, *Mono- and Dibasic Sodium, Potassium and Ammonium Phosphites*).

As stated above, since November 17, 2010, the PMRA is implementing a more flexible approach to assessing product claims as a result of Regulatory Proposal PRO 2010-07, *Value Guidance – Benefit Information and Use History*, with emphasis on the value aspect. It is the PMRA's position that since Phostrol Fungicide is demonstrated to be effective against the pink rot pathogen (*Phytophthora erythroseptica*) in the foliar application studies, efficacy against the pathogen has been established. The value contribution is that with an in-furrow application being made early in the season, it will contribute to keeping the pathogen's population lower than without an application, and may lead to reduced foliar and post-harvest fungicide use later in the season. In addition, since Phostrol Fungicide is recommended to be applied in a tank-mix with other fungicides registered for in-furrow applications, there is also the contribution to resistance management for those other active ingredients. In conclusion, the PMRA has determined that there is value to a single in-furrow application of Phostrol Fungicide; however, additional confirmatory value evidence was requested to demonstrate consistency in product performance. The claim for suppression of pink rot (*Phytophthora erythroseptica*) on potatoes when Phostrol Fungicide is applied once as an in-furrow application is supported.

Comment # 4: For the claim of control of late blight (*Phytophthora infestans*) on potatoes when applied at 2.9-11.6 L/ha Phostrol Fungicide, the commenter requested the removal of the 2.9 L/ha rate of Phostrol Fungicide, citing their belief that there was insufficient data submitted to support this claim. The commenter stated that they believe too low and/or too few applications of phosphite-based products are insufficient to control late blight or pink rot. The commenter also cited the fact that due to economic pressures, growers will apply sub-label rates, or just the low application rate, under all disease pressures. The commenter submitted evidence based on a similar phosphorus acid-based product which was assessed in a separate application.

PMRA Response: The PMRA assesses a product's value for each crop and disease claim individually, reviewing the information that was submitted at the time of the evaluation. The PMRA does not refer to data submitted from previous applications for comparison purposes. Two efficacy trials, testing eight applications of the lower Phostrol Fungicide rate under high disease pressures, resulted in disease control levels and tuber yields similar to a registered commercial standard. Results demonstrated that applying Phostrol Fungicide at the low rate in alternation with other fungicides registered for control of late blight also resulted in acceptable disease control, therefore, it can be used in conjunction with other fungicides as part of a season-long control program. In addition, it was recommended that Phostrol Fungicide be applied in a tank mix with other fungicides registered for control of late blight. Therefore, Phostrol Fungicide has additional value in that it contributes towards resistance management of late blight for other active ingredients.

With respect to the commenter's position that for economic reasons, growers will apply the lowest label rate, or sub-label rates of a product, regardless of the disease pressures found in the field, the PMRA cannot address that point. The PMRA is charged with recommending product rates that are effective and appropriate under a range of disease pressures and environmental conditions. Label wording is provided which outlines when to apply the low rate and what application interval is appropriate under low or high disease pressures.

It is the PMRA's opinion that for the claim of control of late blight (*Phytophthora infestans*) on potatoes when applied at 2.9-11.6 L/ha Phostrol Fungicide, there is value to keeping the low rate on the product label, especially when used under conditions of low disease pressures.